The Use and Abuse of Desiccated Thyroid*

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WHILE desiccated thyroid is the oldest and perhaps the most specific therapeutic agent employed in clinical endocrinology, there is still considerable misunderstanding regarding the indications for its use, the dose to be employed, and its untoward manifestations.

Because of its specificity in frank hypothyroidism, the results obtained from the administration of desiccated thyroid may be considered, within definite limits, as a valuable diagnostic criterion. This statement is qualified because of the large number of physiological and psychological variants to be considered before a definite diagnosis can be made in the obscure or borderline case. Let us consider the physiological problems first.

For many years observers interested in metabolic disorders have known that the level of oxygen consumption — as indicated by a so-called basal metabolic rate—is not a true, or perhaps I should say, not an infallible measure of thyroid function. It is also known that some individuals are refractory to moderate doses of thyroid and that not infrequently their basal metabolic rates fall to levels lower than those encountered before thyroid ingestion. This phenomenon was further elucidated by Farquharson and Squires.[1] They studied patients with normal or moderately depressed basal metabolic rates, who had normal cholesterol values and no clinical evidence of hypothyroidism. Some of the subjects were under treatment for obesity; the others were the ordinary mill run of patients with vague symptom complexes, rarely found to be on a metabolic basis.

The authors noted that when thyroid was administered in relatively small doses, the basal metabolic rates were promptly increased, but after two or three months they usually fell to, or close to, the initial level. Continued administration of larger doses (sufficient to raise the basal metabolic rates of myxedematous patients to normal levels), produced another rise in the basal metabolic rate, followed by a gradual decrease (Fig. 1). With still larger doses, the rate rose, and remained at an elevated level. When the excessive dose of thyroid was withdrawn after prolonged administration, the basal metabolic rate fell rapidly to a point below the patient's initial level. At the same time the patient complained of mild weakness, lassitude and fatigue, the pulse became slow, and there were other indications of deficient thyroid activity. The above results were obtained whether the patients were losing or gaining weight during therapy. Riggs, Man, and Winkler have also shown that the blood iodine falls to myxedema levels shortly after discontinuing thyroid medication given to normal individuals, and does not return to normal for five or six weeks.[3] Our experiences have been much the same. (Fig. 2.)

This depression of thyroid function accounts for the fact that many physicians give larger and larger doses of thyroid to patients, erroneously diagnosed as hypothyroid, in order to raise the oxygen consumption to levels they consider normal. I have seen many young persons with basal metabolic rates ranging from —15 to —20 and lower, who have been taking from three to eight grains of standard brands of desiccated thyroid daily for a number of years simply because some physician had attempted to elevate the basal metabolic rate to —10 or above. In other words, the physician was treating the basal metabolic rate instead of the patient. As a matter of fact, these normal individuals were actually made hypothyroid by injudicious thyroid administration. When the dose of administered thyroid reaches a point where it overcomes the artificially created deficiency and speeds up general body metabolism to an abnormal degree, the physician frequently considers his treatment a success. If, however, the basal metabolic rate cannot be raised to —10 or thereabouts without producing some evidence of thyroid intoxication, he usually asks for help.

In contrast to this refractoriness, true hypothyroid patients are sensitive to ingested thyroid and the basal metabolic rate promptly rises following the administration of even small doses (one-half to one grain daily). Rarely more than two grains of thyroid are necessary to maintain the severe myxedema patient in normal metabolic balance and some such individuals keep in perfect health on much less, namely, from one-half to one and one-half grains daily. (Fig. 3.)

In addition to the above, the technical flaws incident to the arrival at a figure representing the supposed basal metabolic level are legion. It might be well to again mention the vagaries of the patient, the machine and the technician, not to speak of such apparently minor items as the cold bed, the noisy or stuffy room, and the fact that most individuals suffer from claustrophobia.

If, then, one cannot depend upon the figure or even the interpretation of the figure when it is correct, what place has the basal rate in the diagnosis of hypothyroidism? In the adult it is one of a triad of laboratory devices designed to either verify or refute one's clinical impressions of a given case. The other two are the blood organic iodine and the blood

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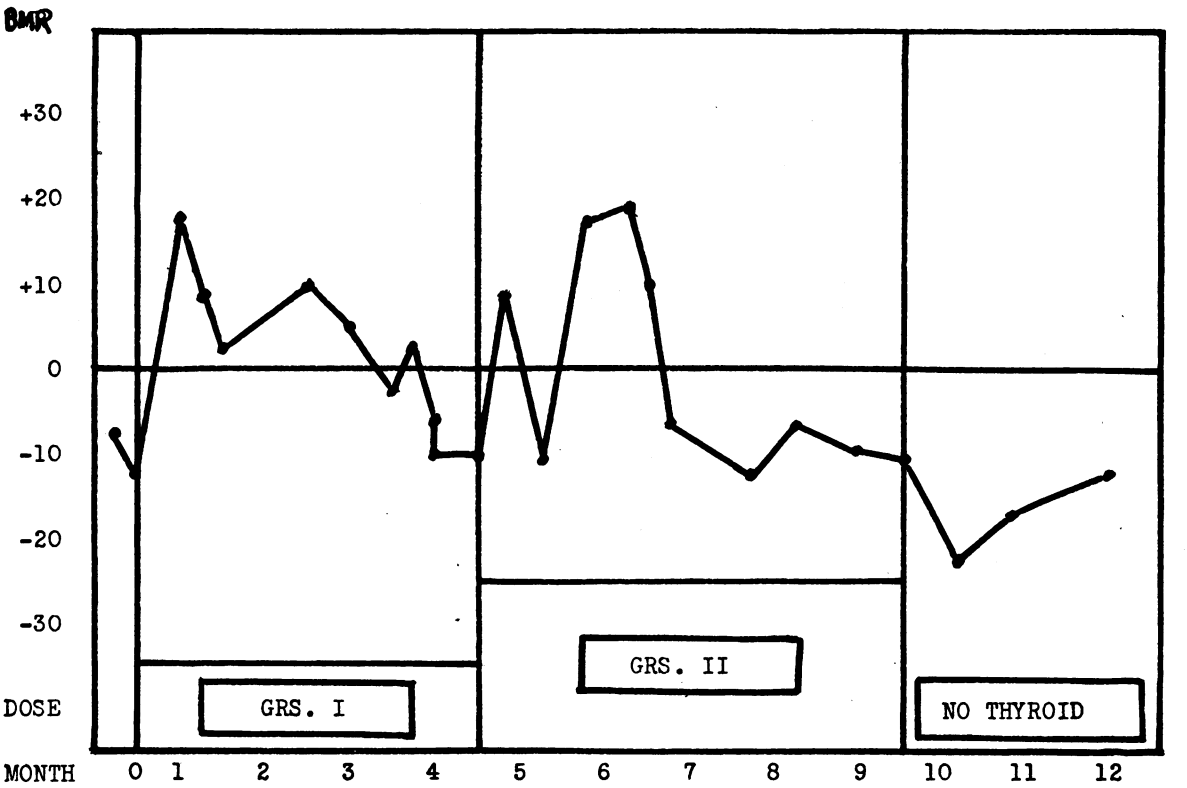

Figure 1.—Effect of Small Doses of Desiccated Thyroid on Basal Metabolic Rate of Normal (Non-Hypothyroid) Individual. (After Farquharson & Squires).

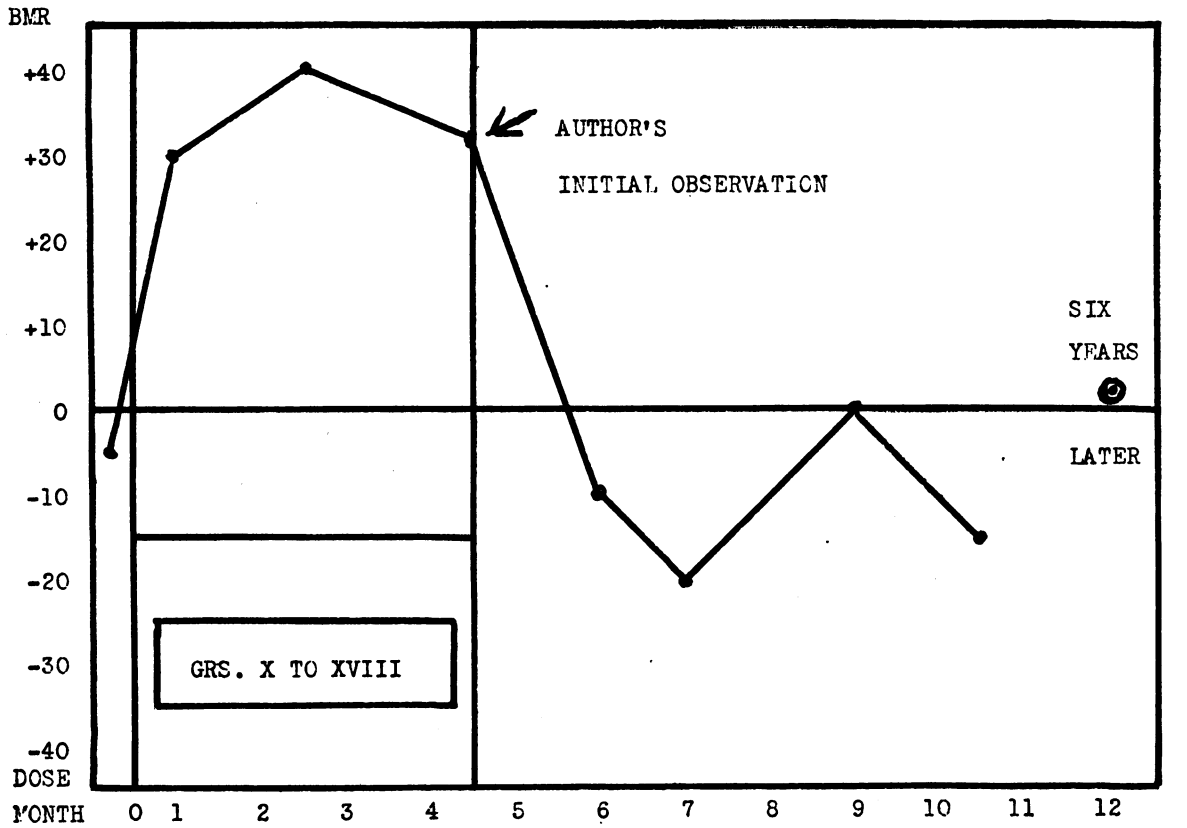

Figure 2.—Effect of Large Doses of Desiccated Thyroid on the Basal Metabolic Rate of a Normal (Non-Hypothyroid) Individual. (Author's Observation).

cholesterol. However, the iodine and cholesterol values, when considered alone, are subject to the same criticism, both as to the vagaries of the laboratory technique and the danger of dogmatic interpretation. In childhood the bone age and urinary excretion of creatin are also helpful diagnostic procedures.

While bone age continues to be the most objective evidence of the developmental status of the child, not all children with retarded bone age suffer from hypothyroidism.[4] Unfortunately, this writer has seen such a procedure endowed with as much diagnostic dogmatism as the basal metabolic rate. The same may be said of the urinary excretion of creatin in childhood. While all severely hypothyroid children excrete little or no creatin when not taking thyroid, not all children with poor urinary creatin excretion are hypothyroid. As in the case of the bone age, the urinary creatin excretion argues either for or against hypothyroidism in an otherwise carefully considered case.[5]

Even when the symptoms are vague and unorthodox, it is not difficult to arrive at a fairly prompt and accurate conclusion in the doubtful case of hypothyroidism, if a patient is not then or has not recently been taking thyroid. If the patient has taken thyroid recently (within three months) and he wonders if he really requires it—in other words, if he consults one for an opinion regarding his true metabolic status—it is necessary to discontinue the thyroid for at least three months so that the basal metabolic rate, iodine and cholesterol values can return to their non-treated or original levels. It is even better to study the patient while he is taking the thyroid and then check these values against those taken three months and even six months later. Many overzealous individuals who have been taking thyroid for years because of fatigue or depression or falling hair, or any one of a hundred complaints, could then be properly instructed to discontinue the thyroid because it is adding nothing to their welfare. However, it is sometimes difficult to get patients off of such medication, since they have created a temporary deficiency by overmedication. After the first shock of a-medication the normal individual gradually returns to his original metabolic status and feels much as he did when taking thyroid.

For example, A. L., age 19, consulted us December 12, 1945, because of nervousness and because she wished her thyroid medication adjusted. The patient had been taking thyroid for eight years, starting with grain 1 and going up to grains 4 daily. The basal metabolic rate was said to have been —30 originally (1937). As the thyroid dosage was increased, the basal metabolic rates rose slightly but were difficult to bring to normal. While the patient felt fairly well when taking grains 4 of thyroid daily, the basal metabolic rate would not go above —17.

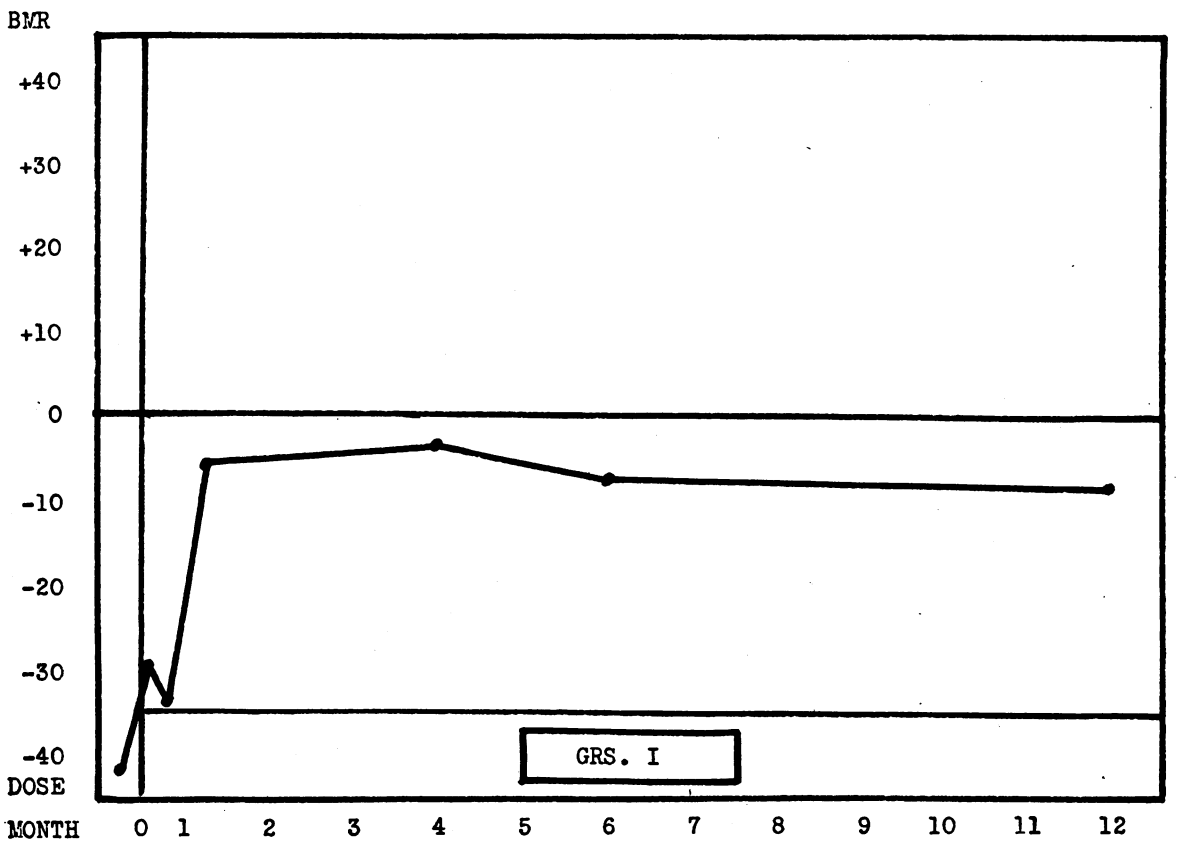

Figure 3.—Effect of Small Doses of Desiccated Thyroid on the Basal Metabolic Rate of Hypothyroid Patient (Myxedema). Modified After Farquharson & Squires.

Attempts to raise the basal metabolic rate above —17 with larger doses of thyroid always produced nervousness. Nine weeks before consulting us, the patient had been taken off of thyroid altogether by another physician. She became so cold and lethargic that she asked us to act in the capacity of a referee. To take thyroid or not to take it—that was the question. Our original observations were as follows: Basal metabolic rate —17, blood cholesterol 250 milligrams, blood organic iodine 3.2 micrograms. In spite of the low metabolic status, we advised her not to resume thyroid, but to come in again in three months for further study. At this time the basal metabolic rate was —10, blood cholesterol 140 milligrams, and blood organic iodine 5.7 micrograms—all normal findings. Still later, the basal metabolic rate was —4. The patient lost most of her nervousness and maintains a normal metabolic status without thyroid.

In contrast, the truly hypothyroid individual gradually regains his old spontaneous symptoms and may even develop myxedema. In the latter case the laboratory, if indicated at all, will soon verify the clinical impression and thyroid should be resumed.

The psychological factors to be considered are no less important, if not so confusing. What of the patient who complains of fatigue, but in whom no laboratory or clinical diagnosis of hypothyroidism can be made? Will thyroid alleviate the fatigue? It will not. Such patients have psychogenic or nutritional factors to account for their difficulties or possibly some hidden focus of infection. The same may be said of constipation, coldness, rough skin and so on ad infinitum. It is true that certain menstrual disorders, amenorrhea, oligomenorrhea, and menorrhagia are occasionally the result of thyroid deficiency and that some such afflicted individuals improve on thyroid. It seems a pity, however, that the nine sufferers whose etiology is not on a hypothyroid basis must be filtered out by injudicious thyroid administration in order to catch the one who really profits from such a regime. Such empiricism is excusable only when the patient is under careful scrutiny for a limited period. It is not unusual to see patients who have been taking thyroid for so long they have forgotten why it was originally administered.

In doubtful cases when one suspects hypothyroidism and does not have recourse to meticulous laboratory studies but must depend in a large measure upon his clinical judgment, I feel he should limit the therapeutic test period to no longer than two months. One should first take a careful history, outlining each and every one of the patient's complaints. If there are no immediate contraindications, such as coronary disease, a badly decompensated heart, active tuberculosis, etc., he may begin by giving the patient a half grain of a standard brand of desiccated thyroid once a day. Each week after this, increase the daily dose by a quarter of a grain until two grains are reached, and continue on this dosage for the balance of the two months. If, at the end of this period the patient is not enthusiastic about the results, he does not suffer from hypothyroidism, and the thyroid should be discontinued. If the majority of the symptoms have been alleviated, the patient is most likely hypothyroid and the minimum dose required (usually something between one and two grains a day) to keep him in good health, should be continued. While the patient should be observed every week during this trial period, one is justified in seeing him only at long intervals after the dose has once been established. One should take into account, of course, that in the case of the normal individual a minor state of hypothyroidism has been temporarily produced and the patient will need a few weeks to adjust to the let-down from thyroid withdrawal.

Other psychological factors of relatively minor importance might be mentioned. Since individuals who need thyroid, especially those with myxedema, are quite sensitive to ingested thyroid, the physician should be wary of the patient's reactions. I have seen patients with frank myxedema convince their physicians that they were so intolerant to thyroid that even one-tenth of a grain would produce severe nervous symptoms. In such a case it is best to give thyroid in a colored capsule and call it something else.

Some years ago I was called in consultation regarding such a patient. The woman, obviously suffering from myxedema, had convinced her local physician, as well as others in several large clinics throughout the country, that she was very intolerant of thyroid (which indeed she may have been temporarily). A pink capsule, ostensibly containing the thyrotropic hormone, but actually containing one-half grain of thyroid, completely rehabilitated the woman in a few months. The physician was later told of the deception and became quite angry.

Some patients complain that thyroid taken at night keeps them awake. I used to explain how such a reaction would be improbable. I now find it saves time and breath to tell them to take it in the morning. While we are on the subject I can see no reason why thyroid should be given oftener than once a day at the most convenient hour for the patient.

Thyroid is used consistently and erroneously in the treatment of obesity. In my judgment there is no such disorder as thyroid obesity; in fact more hypothyroid sufferers are thin than fat. If one has myxedema he will lose weight while taking thyroid until the myxedematous infiltration is metabolized and the by-products of his faulty protein metabolism are eliminated. After this point, thyroid will merely act as it does in the normal individual. Since we have pointed out that thyroid will depress the function of the gland, it could conceivably enhance rather than alleviate the deposition of fat. If one administers thyroid to the point where the metabolism is actually stimulated, increased appetite and nervousness often add to the patient's discomfort.

I have seen numerous obese individuals in whom physicians were trying to force a result by administering large doses of thyroid. One such patient was actually given eighteen grains of a very potent

desiccated thyroid daily for over a year. She was also placed on an eight-hundred calorie diet. If it had not been for the fact that she stole from fifteen-hundred to two thousand calories a day in addition to the diet, she would not have survived. While her basal metabolic rate rose to only +37 she became severely decalcified and lost several teeth through demineralization of the alveolar processes. The weight loss for that hectic year was eleven pounds. After thyroid was entirely withdrawn, the basal metabolic rate came back to around —12 in about six months, during which period she also lost forty pounds on a restricted diet. This is an outstanding example of the abuse the thyroid gland will tolerate and apparently still go back to a normal physiological status. (Fig. 2.)

It is ironical that while I was writing this paper a case report came to my attention in which an obese woman stole and ingested 100 grains of thyroid a day for over a year. She was ultimately discovered to be insane and died suddenly without benefit of autopsy. Goldfinger's [2] rather bizarre conclusion to this interesting case was that: "It is possible that too much conservatism in thyroid dosage has been used by the medical profession in the past. The factor of safety is large, and although exceeded in this case, it is suggested that a much higher dose (U.S.P.) may be used where the thyroid effect is desired. Further work upon the amount of thyroid necessary to increase the metabolic rate would seem to be in order to establish effective, but non-toxic dosage levels."

With such conclusions in the literature, it seems almost futile to preach conservatism.

Whether or not thyroid is indicated in the majority of individuals past middle age is problematical. Certainly the general metabolic processes, including thyroid function, are on the wane. This writer feels that much depends upon the arterial status and the level of the blood cholesterol. Blood cholesterol tends to rise in middle age and when no hepatic or renal disturbance can be demonstrated in one with elevated cholesterol levels, one is perhaps justified in administering small doses of thyroid over a long period without other verifying evidence of hypothyroidism.

While the injudicious use of large doses of thyroid in coronary disease and cardiac decompensation is to be deplored; one should not forget that some coronary disease is merely the end result of long-standing cholesteremia incident of hypothyroidism and some cardiac decompensation is due to a myxedematous infiltration of the myocardium. In either instance thyroid should be administered slowly, at the proper time, and in small doses. The shock of a too rapidly elevated metabolism is sometimes more than a weakened myocardium can tolerate. In such cases, the collaboration of an experienced cardiologist in treatment is paramount.

In childhood small doses of thyroid are anabolic while large doses are catabolic. When indicated nothing works in as spectacular a manner as thyroid in problems of growth and development. The most outstanding stimulation of growth I have obtained has been with doses ranging from one to two grains of thyroid daily. Larger doses have been advocated in cretinism, but it is my feeling that when two grains of thyroid will not rehabilitate a hypothyroid child, twice that much will have no better effect. If the dose is too high, calcium will be withdrawn rather than deposited, and the patient will remain on a negative mineral balance. Here again, if the patient is not truly hypothyroid, growth will not be stimulated and thyroid is more than useless.

Mixtures of thyroid and other medicaments are, in my judgment, bad medicine, unless it is first established that the patient really needs thyroid, and, second, what dose is required. Then and then only is the physician justified in adding another potent preparation such as benzedrine to a mixture designed to treat any disorder. Such preparations as we see for obesity containing thyroid, benzedrine, atropine, aloin, and what have you, are three steps back of the right direction, and should be left for our less scrupulous brothers, the irregular. When thyroid is combined with inert material such as whole ovary, testis, anterior pituitary, spleen, etc., your patient pays a fancy price for the leavings of the slaughter house and gets thyroid function and nothing else. When prescribing other hormones to a patient who also requires thyroid, give the most potent preparation available separately, so that you can evaluate each step of the treatment. All standard brands of desiccated thyroid are probably efficacious, but not necessarily grain for grain. It is best to employ one brand until one is thoroughly familiar with its potency and action. Then and then only are therapeutic comparisons of clinical value.

To sum up briefly then, thyroid is a specific drug in hypothyroidism. The administration of thyroid to normal individuals depresses thyroid function. A diagnosis of obscure hypothyroidism can be made both clinically and from the laboratory if a number of criteria are considered. Thyroid dosage in all cases, and in both children and adults, ranges from one-half to three grains a day. Small doses of thyroid are anabolic and large doses catabolic particularly but not exclusively in children. Small doses of thyroid probably postpone the aging process in middle-aged adults with moderately high cholesterol values. Thyroid should be administered alone until its full effect on a given individual is well established.

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